Press release

Leqembi (lecanemab) authorized for early Alzheimer's disease in Great Britain

Stockholm, Sweden August 22, 2024 – BioArctic AB (publ) (Nasdaq Stockholm: BIOA B) partner Eisai announced today that Leqembi® (brand name, generic name: lecanemab) has been granted Marketing Authorization by the Medicines and Healthcare products Regulatory Agency (MHRA) in Great Britain, for the treatment of mild cognitive impairment (MCI) and mild dementia due to Alzheimer's disease (AD) in adult patients that are apolipoprotein E ε4 (ApoE ε4)[1] heterozygotes or non-carriers.[2] Lecanemab becomes the first the medicine which targets an underlying cause of the disease, to be authorized in a country in Europe.

"The decision from MHRA to authorize lecanemab is an important step forward for eligible patients in Great Britain who could now for the first time gain access to a treatment which in studies has been shown to slow the progression of early Alzheimer's disease. For Alzheimer's disease patients, time is the most valuable asset, and access to new treatments has potential to offer them just that," said Gunilla Osswald, CEO at BioArctic.

Lecanemab selectively binds to Aβ aggregate species, with preferential activity for toxic Aβ protofibrils[3] (as well as fibrils, which are a major component of Aβ plaques). Lecanemab binds to these aggregate Aβ species to neutralize and clear them from the brain. [4,5,6]

The approval was mainly based on Phase 3 data from the global Clarity AD clinical trial, in which the medicine met its primary endpoint and all key secondary endpoints with statistically significant results.[4] In the indicated population in Great Britain, the most common adverse reactions were infusion-related reaction, amyloid-related imaging abnormalities with hemorrhage (small spots of bleeding) (ARIA-H)[7], fall, headache and amyloid-related imaging abnormalities with cerebral edema (build-up of fluid) (ARIA-E)[8].[2]

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[1] Apolipoprotein E is a protein involved in the metabolism of fats in humans. It is implicated in Alzheimer's disease.
[2] Lecanemab Great Britain Summary of Product Characteristics
[3] Protofibrils are large Aβ aggregated soluble species of 75-5000 Kda
[4] van Dyck, H., et al. Lecanemab in Early Alzheimer's Disease. New England Journal of Medicine. 2023;388:9-21. https://www.nejm.org/doi/full/10.1056/NEJMoa2212948
[5] Johannesson, M., et al. Lecanemab demonstrates highly selective binding to Aβ protofibrils isolated from Alzheimer's disease brains. Molecular and Cellular Neuroscience. 2024;130:103949. https://doi.org/10.1016/j.mcn.2024.103949
[6] Sehlin, D., et al. Large aggregates are the major soluble Aβ species in AD brain fractionated with density gradient ultracentrifugation. PLoS One. 2012;7(2):e32014. https://doi.org/10.1371/journal.pone.0032014
[7] ARIA-H: amyloid-related imaging abnormalities with hemorrhage (combined cerebral microhemorrhages, cerebral macrohemorrhages, and superficial siderosis).
[8] ARIA-E: amyloid-related imaging abnormalities with oedema (edema/effusion).

It is estimated that 982,000 people live with dementia in the UK[9] and that Alzheimer's disease is the cause in 60-70% of people with dementia.[10] These numbers are expected to increase even further with an aging population.

Eisai is working collaboratively with the National Institute for Health and Care Excellence (NICE), the Scottish Medicines Consortium (SMC) and the National Health Service (NHS) to make this medicine available to eligible people living with early Alzheimer's disease as soon as possible.

Lecanemab is the result of a long-standing collaboration between BioArctic and Eisai, and the antibody was originally developed by BioArctic based on the work of Professor Lars Lannfelt and his discovery of the Arctic mutation in Alzheimer's disease. Eisai serves as the lead of Leqembi development and regulatory submissions globally with both Eisai and Biogen co-commercializing and co-promoting the product and Eisai having final decision-making authority. BioArctic has the right to commercialize lecanemab in the Nordic region and pending European approval Eisai and BioArctic are preparing for a joint commercialization in the region.

This information is information that BioArctic AB (publ) is obliged to disclose pursuant to the EU Market Abuse Regulation. The information was released for public disclosure, through the agency of the contact persons below, on August 22, 2024, at 11.05 a.m. CET.

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About lecanemab (Leqembi®)
Lecanemab is the result of a strategic research alliance between BioArctic and Eisai. It is a humanized immunoglobulin gamma 1 (IgG1) monoclonal antibody directed against aggregated soluble (protofibril) and insoluble forms of amyloid-beta (Aβ).

Lecanemab's approval in Great Britain was primarily based on Phase 3 data from Eisai's global Clarity AD clinical trial, in which it met its primary endpoint and all key secondary endpoints with statistically significant results.[2,4] Clarity AD was a Phase 3 global, placebo-controlled, double-blind, parallel-group, randomized study in 1,795 patients with early AD (MCI or mild dementia due to AD, with confirmed presence of amyloid pathology), of which 1,521 were in the indicated population in the label in Great Britain (ApoE ε4 heterozygotes or non-carriers).[2] Of the total number of patients randomized 31% were non-carriers, 53% were heterozygotes and

[9] Alzheimer's Society. 2024. The economic impact of dementia. Available at: https://www.alzheimers.org.uk/about-us/policy-and-influencing/dementia-scale-impact-numbers. Last accessed: August 2024.
[10] World Health Organization. 2023. Dementia. Available at: https://www.who.int/news-room/fact-sheets/detail/dementia. Last accessed: August 2024

16% were homozygotes.1 The treatment group was administered lecanemab 10 mg/kg bi-weekly, with participants allocated in a 1:1 ratio to receive either placebo or lecanemab for 18 months.[2]

The primary endpoint was the global cognitive and functional scale, CDR-SB.[2] In the Clarity AD clinical trial, treatment with lecanemab, in the indicated population in Great Britain (ApoE ε4 heterozygotes or non-carriers), reduced clinical decline on CDR-SB by 33% at 18 months compared to placebo.[2] The mean CDR-SB score at baseline was approximately 3.2 in both groups.[2] The adjusted least-squares mean change from baseline at 18 months was 1.15 with lecanemab and 1.73 with placebo (difference, −0.58; 95% confidence interval [CI], −0.81 to −0.34; P<0.00001).[2] CDR-SB is a global cognitive and functional scale that measures six domains of functioning, including memory, orientation, judgement and problem solving, community affairs, home and hobbies, and personal care.

In addition, the secondary endpoint from the AD Cooperative Study-Activities of Daily Living Scale for Mild Cognitive Impairment (ADCS-MCI-ADL), which measures information provided by people caring for patients with AD, noted 39% less decline compared to placebo at 18 months.1 The adjusted mean change from baseline at 18 months in the ADCS-MCI-ADL score was −3.5 in the lecanemab group and −5.7 in the placebo group (difference, 2.2; 95% CI, 1.3 to 3.1; P<0.00001).1 The ADCS-MCI-ADL assesses the ability of patients to function independently, including being able to dress, feed themselves and participate in community activities.

In the indicated population (ApoE ε4 heterozygotes or non-carriers), the most common adverse reactions were infusion-related reaction (26%), ARIA-H (13%), fall (11%), headache (11%) and ARIA-E (9%).1

Lecanemab is licensed in the U.S., Japan, China, South Korea, Hong Kong, Israel, the United Arab Emirates and Great Britain and marketed in the U.S., Japan and China. Eisai has also submitted applications for approval of lecanemab in 10 countries and regions, including the European Union.

▼: This medicine is subject to additional monitoring. This will allow quick identification of new safety information.

About the collaboration between BioArctic and Eisai
Since 2005, BioArctic has a long-term collaboration with Eisai regarding the development and commercialization of drugs for the treatment of Alzheimer's disease. The most important agreements are the Development and Commercialization Agreement for the lecanemab antibody, which was signed 2007, and the Development and Commercialization agreement for the antibody Leqembi back-up for Alzheimer's disease, which was signed 2015. In 2014, Eisai and Biogen entered into a joint development and commercialization agreement for lecanemab. Eisai is responsible for the clinical development, application for market approval and commercialization of the products for Alzheimer's disease. BioArctic has the right to commercialize lecanemab in the Nordic region under certain conditions and is currently preparing for commercialization in the Nordics together with Eisai. BioArctic has no development costs for lecanemab in Alzheimer's disease and is entitled to payments in connection with regulatory approvals, and sales milestones as well as royalties on global sales.

About BioArctic AB
BioArctic AB (publ) is a Swedish research-based biopharma company focusing on innovative treatments that can delay or stop the progression of neurodegenerative diseases. The company invented Leqembi® (lecanemab) – the world's first drug proven to slow the progression of the disease and reduce cognitive impairment in early Alzheimer's disease. Leqembi has been developed together with BioArctic's partner Eisai, who are responsible for regulatory interactions and commercialization globally. In addition to Leqembi, BioArctic has a broad research portfolio with antibodies against Parkinson's disease and ALS as well as additional projects against Alzheimer's disease. Several of the projects utilize the company's proprietary

BrainTransporter™ technology, which has the potential to actively transport antibodies across the blood-brain barrier to enhance the efficacy of the treatment. BioArctic's B share (BIOA B) is listed on Nasdaq Stockholm Large Cap. For further information, please visit www.bioarctic.com.

About NHS, NICE and SMC

The National Health Service (NHS) is a public healthcare system with the principle of providing free medical services to citizens. The National Institute for Health and Care Excellence (NICE), and the Scottish Medicines Consortium (SMC) are independent bodies that carry out assessments on the status of all newly licensed medicines, all new formulations of existing medicines and new indications for established products regarding their health benefits and price justification as an advisory boards to the National Health Service (NHS) about whether or not a newly licensed drug should be accepted for use under national health insurance**.**